REMARKS

I. Claim Status and Support for the Claim Amendments

Reconsideration of this Application is respectfully requested. Claims 1-7, 9-17, 20, 22, 23-27 and 29 are pending in the application. Claims 8, 18-19, 21, 23 and 28 have been canceled. Claim 29 is newly added. No new matter is introduced by way of these amendments, and their entry is respectfully requested.

II. The Rejection under 35 U.S.C. § 112, second paragraph is Moot

The Office Action rejected claim 28 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. As noted, Applicants have canceled claim 28. Accordingly, the indefiniteness rejection is rendered moot. Applicants request reconsideration and withdrawal of this rejection.

III. Rejections under 35 U.S.C. § 103(a)

A. The Rejection of Claims 1-7, 9-17, 20 and 22-25 under 35 U.S.C. §103(a) is Moot

The Office Action rejected claims 1-7, 9-17, 20 and 22-25 under 35 U.S.C. § 103(a) as allegedly being unpatentable over Chang et al (US 5,270,169) in view of Walter et al., (Stimulation of human cytotoxic T cells with HIV-1-derived peptides presented by recombinant HLA-A2 peptide complexes, *International Immunology*, vol. 9, No. 3, pp. 451-459, 1997). Applicants assert that the remarks traverse and render moot the obviousness rejections over Chang et al. and Walter et al. Applicants request reconsideration and withdrawal of the obviousness rejection of claims 1-7, 9-17, 20 and 22-25.

According to the Office Action, "[i]t would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate a recombinant HLA antigen and the

corresponding reagents as taught by Walter et al. into the method of Chang et al. because Chang et al. teaches that the HLA antigen can be a synthetic HLA antigen and Walter shows that recombinant complexes contain native epitopes, consistent with the presence of correctly folded molecular complexes."

Chang involves the detection of HLA immune complexes through binding of C1q moieties attached to solid supports. C1q is a collagen-like hexamer containing a central core or stalk, and globular protein heads that are responsible for the binding of immunoglobulins (IgM, and IgG). Chang uses HLA antigens in order to facilitate immune complex formation for C1q binding (*citing* Abstract "[t]he immune complexes are preformed, or formed by adding HLA antigens to a biological sample containing antibodies to HLA…The immune complexes bind to C1q, and are then detected by the addition of a labeled reagent"). Accordingly, adding recombinant HLA antigens taught by Walter to the method in Chang results in a generic C1q-bound immune complex that happens to contain recombinant HLA antigens. That is not what is being claimed.

Claim 1, for example, is directed to a method of detecting the presence of one or more allele specific anti-Major Histo-Compatibility Complex (MHC) antibodies in a body fluid sample comprising contacting said sample with one or more recombinant MHC molecules which each bind to a different allele specific MHC antibody, if present in said sample, and detecting binding or absence of binding of said one or more allele specific antibodies to said recombinant MHC molecules, wherein each of said one or more allele specific antibodies is specific for a particular naturally occurring MHC allele and binds to only one of said one or more recombinant MHC molecules which contains one or more epitopes of said naturally occurring MHC allele. Accordingly, detection is based on specificity of the MHC molecule.

Notwithstanding the fundamental differences in detection modalities, Applicants submit that one skilled in the art would not have any reason to combine Chang and Walter period, let alone arrive at something remotely similar to the present claims. Walter is directed to the stimulation of human cytotoxic T cells with HIV-1-derived peptides presented by recombinant HLA-A2 peptide-bead complexes, essentially the creation of an HIV vaccine or therapy. In

attempting to make the vaccine, Walter creates recombinant HLA-A2 peptides that are conjugated to silica beads. Walter uses monoclonal antibodies for analysis of the complexes, such as in HPLC. Pgs 452-453. Walter does not suggest a sample detection assay from a biological specimen similar to that described in Chang, who uses of HLA antigens in the formation of immune complexes that are subsequently detected by C1q moities described above. The only true rationale for combining Chang and Walter to arrive at anything remotely similar to the present claims is grounded firmly in hindsight reconstruction.

In addition, the Office Action states that "Walter et al. disclose that a recombinant MHC molecule can contain native epitopes, and can be immobilized and bound by antibody" or a support, such as silica. Chang is based on the formation of immune complexes by addition of bare HLA antigens which are bound through C1q molecules. Accordingly, correct complex formation is critical in Chang and it is highly unlikely that one would want to functionalize the HLA antigens with a solid support or antibody, especially according to the aforementioned nonselective immobilization techniques in Walter, which could at best attenuate or alter if not altogether block the formation of complexes for C1q binding.

Accordingly, Walter et al. and Cheng et al., fail to render obvious claims 1-7, 9-17, 20 and 22-25. Applicants respectfully request reconsideration and withdrawal of the obviousness rejection under Walter et al. and Chang et al.

B. The Rejection of Claims 24-28 Under 35 U.S.C. §103(a) is Moot

The Office Action of 5 December 2006 rejected claims 24-28 under 35 U.S.C. 103(a) as allegedly being "unpatentable over Chang et al in view of Walter et al as applied to claims 1-7, 9-17, 20 and 22-24 above, and further in view of Luxembourg et al." The Office Action alleges that Luxembourg et al. "disclose recombinant MHC molecules which are biotinylated to provide attachment to a solid support coated with avidin." The Office Action further alleges that "Luxembourg et al disclose that the use of this avidin-biotin system provides for the isolation of peptides such as antibodies." As describe above, Chang et al. and Walter et al. fail to render obvious claims 1-7, 9-17, 20 and 22-24. Luxembourg does nothing to cure their deficiencies.

Accordingly the combined teachings of Chang et al., Walter et al. and Luxembourg et al. do not render obvious claims 24-28, which are dependent thereon.

C. The Rejection of Claims 21 and 23 Under 35 U.S.C. §103(a) is Moot

The Office Action of 5 December 2006 rejected claims 21 and 23 under 35 U.S.C. 103(a) as allegedly being unpatentable over Walter et al., (Stimulation of human cytotoxic T cells with HIV-1-derived peptides presented by recombinant HLA-A2 peptide complexes, *International Immunology*, vol. 9, No. 3, pp. 451-459, 1997) in view of Boguslaski (US 5,420,016). Applicants point out that claims 21 and 23 are canceled. Accordingly, Applicants respectfully request reconsideration and withdrawal of the obviousness rejection of claims 21 and 23.

Applicants further point out the particularly distinct nature of claims 13 and 29, which involve attachment of the MHC molecule to an ELISA plate. In each of the cited references, binding of the HLA antigen to an ELISA plate would render them inoperable for their intended purpose. Accordingly, withdrawal of the rejection to claims 13 and 29 is earnestly solicited.

IV. Conclusion

In view of the foregoing, Applicants request reconsideration and withdrawal of the rejections over the claimed invention. Should the Examiner believe that further discussion of any remaining issues would advance the prosecution, he or she is invited to contact the undersigned at the telephone number listed below.

The USPTO is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account.

Respectfully submitted,

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